Chelsea's Hope
Lafora Children Research Fund

Lafora Disease Therapeutic Overview

Lafora Disease: An Overview

- Lafora disease is a fatal genetic disorder characterized by progressive myoclonus and epilepsy, rapid neurological deterioration, and childhood dementia.
- Children with Lafora have a genetic mutation in one of two genes: EPM2A or NHLRC1 (EPM2B)
- These two genes make the proteins “laforin” and “malin.” Together, laforin and malin regulate the molecule glycogen, the sugar storage mechanism in our cells.
- When laforin and malin lose their function, glycogen accumulates into “Lafora Bodies,” and cells cannot access the sugar stored inside.

Lafora Disease: Therapies

- There are two primary strategies for developing a therapy for Lafora Disease.
    - Strategy 1: Degrade existing Lafora Bodies
    - Strategy 2: Slow the synthesis of glycogen to prevent Lafora Body formation
- Therapies currently in development
    - Antisense Oligonucleotide (ASO): ASOs are designed to identify and bind to a specific transcribed gene (mRNA). When it binds, it forms a duplex, and the RNA cannot be used to make protein. This results in lower levels of that protein in the patient.
    - Antibody Enzyme Fusion (AEF): An AEF uses an antibody to send a protein where it is needed. The antibody is your “delivery mechanism,” and the enzyme (a protein) will perform the needed function in the patient. AEF is a type of Enzyme Replacement Therapy. The enzyme is made in the lab, and then administered to patients through IV or directly to the brain through ICV injections.
    - Small Molecule Therapy: A small molecule is designed to bind to a specific protein. When it binds to the protein, it prevents the protein from performing its function.
    - Gene Therapy: A treatment that alters gene expression in the patient, either to decrease the expression of a specific protein, or to create a correct version of a mutated protein.
- Basic Stages to Therapeutic Development:
    - Initial design of the therapy
    - *In vitro* and *In situ* testing (in test tubes and cell lines)
    - *In vivo* testing (in animal models)
    - Testing of therapy in Large Mammals
    - Human studies (clinical trials)

Dr. Kit Donohue, Chelsea’s Hope Science Director, provided the overview. Please email her for specific therapeutic pipeline updates at katherine@chelseashope.org.